Recurrent Cystosarcoma Phylloides

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THE TERM *cystosarcoma phylloides,* was first used by Mueller in 1838. Sarcoma comes from the Greek word *sar,* meaning flesh, and *oma,* meaning tumor or neoplasm. By definition, *cystosarcoma* would represent a sarcoma in which the formation of cysts has occurred.

Phylloides is also derived from the Greek *phyllon,* meaning leaf, and *oides,* meaning resemblance. These are the sources of the term *cystosarcoma phylloides,* meaning a fleshy tumor with cyst formation and having what appear, on microscopic examination, as leafy projections. This term is the most commonly used for tumors of this kind, although they are also called "giant cell fibroadenoma."

According to Lee and Pack,[4] these tumors were very rare a hundred years ago and are even rarer now because the precursor fibroadenomas are recognized and removed much earlier.

Genesis

There are many possible precursor lesions etiologically incriminated in the development of this tumor. According to Adair and Hermann[1] numerous investigators were able to demonstrate that cystosarcoma could develop from fibroadenoma of the breast.

It would appear Lester and Stout[5] felt that these tumors are sarcomas that develop in fibro-epithelial tumors.

Submitted 17 October 1966.
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Pack and Ariel[6] expressed belief that multiple births and lactation are the most frequent stimuli to the metamorphosis of fibroadenoma into cystosarcoma phylloides. However, there appeared to be no consistent agreement in the literature reviewed as to the exact origin.

Gross Description

These tumors are usually very large, bulky tumors of the breast when first seen. The lesions are usually mobile, circumscribed and discrete from the surrounding breast tissue. There is usually no fixation of the overlying skin, although Lee and Pack[4] noted skin ulceration in 21 of 65 cases reported. There is no nipple retraction and no bleeding from the nipple. Usually the veins overlying the lesions are very prominent. Rarely is there attachment to or invasion of the pectoral fascia. The primary difference between this tumor and the usual fibroadenoma is size. The smaller tumors differ in more proliferative epithelium and coarser, more cellular connective tissue. They may be called miniature cystosarcoma phylloides, the size ranging from 1.0 cm to 20.0 cm.

Cystosarcoma phylloides tumors are made up mainly of intracystic polypoid masses, and owing to their multiple leaf-like laminations have been likened to a cabbage.

Lee and Pack[4] reported the weight of 19 tumors averaged 7.6 pounds. Other investigators have reported breasts containing such tumors weighing as much as 40 pounds.

Microscopic Appearance

There is a very decided variation in the histological appearance of these tumors, both from one part to another of the same tumor and between tumors. Lester and Stout[5] said that in the 58 cases reported by them there were 20 malignant tumors, 10 borderline and 28 benign. They emphasized, as have other investigators, the difficulty in classi-

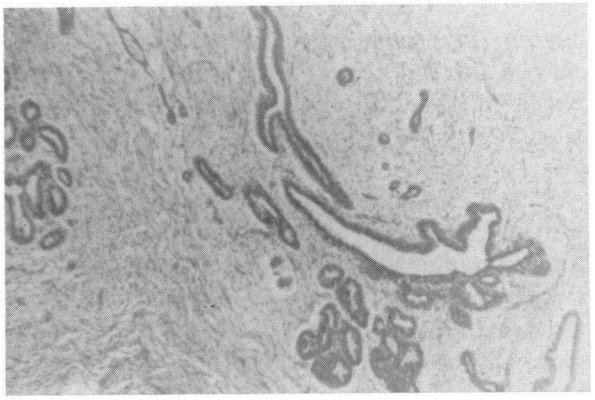

Figure 1.—Cellular stroma containing irregular ductal structures lined by a thick, deeply staining layer of epithelial cells (×53).

fication. They were unable to find any definite clinical guides that are explicitly indicative of malignant change. Size alone was not a basis for prediction.

The main criteria for identifying a tumor as benign is stromal overgrowth in a fibroadenoma pattern. Hyalinization and myxomatous change occur, and there are areas of irregular hyperchromatic nuclei, probably the result of degenerative change. Lee and Pack[4] emphasized the myomatous change in a series of cases they reported. Necrosis is not common. Calcareous deposits and pigment accumulation may occur in the stroma of the tumor. The ducts of the tumor are very dilated and tortuous.

The malignant tumors usually have a highly cellular stroma with considerable pleomorphism and mitotic activity and some invasive properties. In the great majority of cases the malignant change occurs in the connective tissue and not the epithelium. Occasionally bizarre patterns will develop, such as those of squamous carcinoma and osteogenic sarcoma. Tevis and Sunderland,[7] in a report of 77 patients, expressed the opinion that the lesion was more frequently malignant than had been previously suspected.

Clinical Features

According to Adair and Hermann[1] the average age of patients with this tumor is 45 years. Lee and Pack[4] reported the average known duration of the tumor is 6.7 years. The presence of a preexisting lesion is characteristic, as is rapid growth and attainment of large size. Ulceration of the overlying skin is uncommon and, when it does occur, is usually related to trauma. Percursory tumors are present in the vast majority of cases. Cystosarcoma phylloides tumors tend to develop more slowly than carcinoma of the breast and sometimes remain inactive for considerable periods.

Report of a Case

In November 1960, a 35-year-old patient was observed because of a palpable nodule in the axillary tail of the right breast. This particular portion of the breast was quite painful with each menstrual period; and just before she sought medical attention the patient had had increasing discomfort there.

Both breasts were very large and pendulous, and the very prominent, thick breast parenchyma made palpation of any discrete nodules difficult. A presumptive diagnosis of chronic cystic mastitis of the axillary tail of the right breast was made at that time, and the patient was kept under periodic observation.

Approximately nine months later the lesion in the axillary tail of the right breast had become more discrete and appeared to be 3 to 4 cm in diameter, although delineating margins was difficult.

A wedge of breast tissue 6 by 10 cm was excised for biopsy in August 1961, and the diagnosis at that time was "giant fibroadenoma with myxoid stroma (cystosarcoma phylloides) of the breast." Microscopically the lesion was fully circumscribed and had no capsule. The edges of the lesion extended with irregular processes into the surrounding tissues. Because of the benign appearance of the lesion, a quadrant excision of the breast was

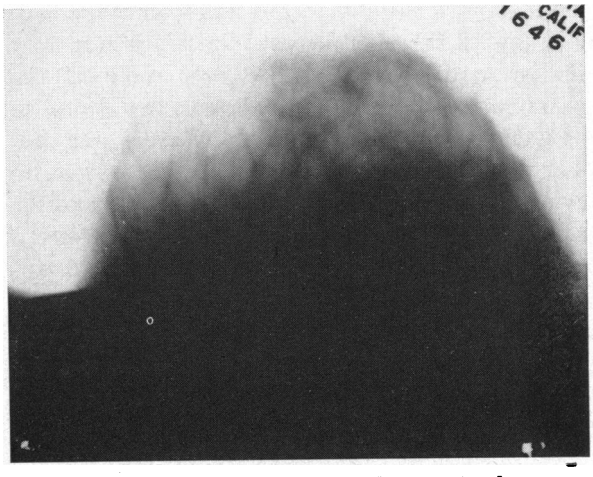

Figure 2.—A 9.0 cm giant fibroadenoma in the upper outer quadrant of the right breast is clearly visible in the mammogram.

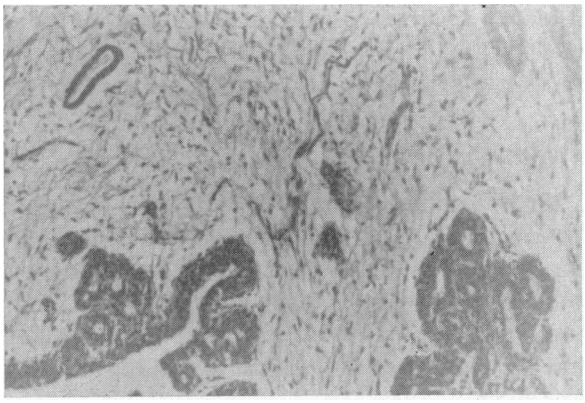

Figure 3.—The cells of the stroma are moderately pleomorphic, as are the epithelial cells lining the ductal structures (×133).

carried out as a definitive treatment and the patient made uneventful recovery.

She was observed periodically thereafter, and when she was examined in September of 1963 there appeared to be some fullness in the right breast, more prominent in the right upper and outer quadrant than elsewhere. Local recurrence of cystosarcoma phylloides was suspected. Mammograms revealed a 9 cm homogeneous, smoothly delineated mass in the upper outer quadrant of the right breast. One fairly large focus of calcification was present in this lesion, and most of the views taken at the time revealed some displacement of fatty tissue around the mass. There was no radiological evidence to suggest malignant disease. There was some compression of the adjacent normal surrounding breast tissue. The radiological appearance was quite characteristic of giant cell fibroadenoma (cystosarcoma phylloides).

On surgical exposure, a rounded, circumscribed mass about 8 cm in diameter was seen in the axillary tail of the right breast. Grossly it was very similar to the mass that had been removed two years earlier. On biopsy the lesion was found to be recurrence of cystosarcoma phylloides, and radical mastectomy was performed. There was no evidence of other tumor within the breast, and the axillary lymph nodes did not appear to be involved with tumor. The tumor, which was spherical, appeared to be completely encapsulated. Microscopically the tumor mass was histologically similar to the biopsy specimen that was excised in 1961. The present lesion showed numerous large and small glandular structures, some of which had a slit-like appearance. There was more hemorrhage and degeneration in the stroma of this lesion and a slight increase in the epithelial hyperplasia, with protrusion of small papillary processes into the gland lumen. The numerous axillary lymph nodes showed decided central fatty replacement of the lymphoid elements and in some nodes an apparent reticulo-endothelial hyperplasia. However, there was no evidence of malignant involvement. The pathological diagnosis was: "Giant fibroadenoma with stromal hemorrhage and degeneration—'Cystosarcoma phylloides.' " The patient made an uneventful recovery. When last seen, approximately five years after the first appearance of a lesion in the right breast, the patient had no recurrent disease.

Prognosis

Lee and Pack[4] reported six cases in a series of 91 cases. Of all the cases of benign cysts reported, none has caused death unless associated with independent carcinoma of the breast. Local recurrence can and does occur, but can be treated by more radical surgical procedures. Lester and Stout[5] reported five cases in which metastasis is known to have occurred, but in none of them was there metastasis to lymph nodes. The mortality rate for malignant cystosarcoma phylloides, including all lesions of unproved derivation, is about 20 to 25 per cent. Metastasis, when it occurs, usually is to the lungs and bone as hematogenous spread, and only in a very rare case is there local lymph node metastasis. Cooper and Ackerman[3] have reported one case of metastasis to lymph nodes. Ackerman also emphasizes the occurrence of the malignant form of these lesions.

Treatment

The preferred surgical procedure for dealing with such lesions ranges from simple local excision of the tumor mass to simple mastectomy to radical mastectomy. All have been used with varying degrees of success. If the lesion is benign and small and well localized to one quadrant of the breast, a wide quadrant excision of the area would appear from most reports to be adequate treatment. If the lesion is benign and large without evidence of lymph node metastasis, simple mastectomy would appear to be the treatment of choice. If it is benign and recurs after local excision, radical mastectomy is advisable, particularly if there is a prominent epithelial component. Radical mastectomy is also recommended for histologically malignant lesions with malignant epithelial elements.

If, as often is the case, histological examination leaves doubt as to whether the lesion is benign or malignant, radical mastectomy is the most prudent course. This is also the treatment of choice when the tumor has extended beyond the capsule.

Haffner[8] has expressed the opinion that these tumors are sarcomas that develop in fibroepithelial tumors, and that when they invade or spread, it is the mesenchymatous elements alone that are responsible. They believe the epithelial elements play only a passive role and never appear in metastatic lesions. The treatment they recommend for malignant cystosarcoma phylloides is extended simple mastectomy in which a wide margin of tissue, including surrounding skin and underlying pectoralis major muscle, is removed.

Adair and Hermann[1] expressed the opinion that, in light of the infrequency of lymph node involvement, radical mastectomy is not justified.

In the literature reviewed, there was little report of the use of radiation therapy in the treatment of this lesion. Adair and Hermann[1] said that there is not enough data on irradiation of a breast sarcoma by which to evaluate its efficacy.

In 1852, Dr. John Birkett[2] in a letter to the editor of *Lancet* said, "The unusual fact of a return of a cystosarcoma of the breast is undoubtedly most rare"; also, "The development of carcinoma subsequent to cystosarcoma is, happily, very rare"; and "Recurrence of cystosarcoma of the breast appears so important in a practical, as well as pathological point of view, that I beg to call your attention to the subject." These words, written in 1852, sound strangely similar to those statements appearing in our present-day literature on this very same rare entity.

Summary

A 35-year-old woman with a palpable nodule in the axillary tail of the right breast had pain in that area on menstruation. A presumptive diagnosis of chronic cystic mastitis was made but nine months later the nodule became more discrete and biopsy showed cystosarcoma phylloides, appearing to be benign. Quadrant excision of the breast was carried out. Two years later, fullness was noted in the right breast and when biopsy of a lesion observed on surgical exposure showed it to be recurrence of cystosarcoma phylloides, radical right mastectomy was done. When last observed, three years later, there was no evidence of recurrence.

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Membranous Glomerulonephritis: Rapidly Fatal Course

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MEMBRANOUS GLOMERULONEPHRITIS has been distinguished histologically from lipoid nephrosis, proliferative glomerulonephritis[2,4] and poststreptococcal glomerulonephritis[5] by its characteristically diffuse thickening of the basement membrane of glomerular capillary tufts, with little proliferation of endothelial cells. Although precise information on the survival of patients with membranous glomerulonephritis after the onset of nephrotic syndrome is lacking, most investigators agree that the condition is relatively stable and progresses slowly, over a number of years, to renal insufficiency.[3,11] The purpose of this report is to record the rapidity with which membranous glomerulonephritis may progress and to point out that in its early stage the disease may be indistinguishable from pure lipoid nephrosis.[4]

Report of a Case

A 69-year-old white woman had been well until August 1963, when a trace of protein was found

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Submitted 27 October 1966.

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